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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

CANELLA, KAREN A

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/646,835

Applicant(s)

MULTHOFF, GABRIELE

Examiner

Karen A Canella

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 31-43, 45-56 and 58-60 is/are pending in the application.
- 4a) Of the above claim(s) 49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 31-41 is/are allowed.
- 6) ☐ Claim(s) 42, 43, 45-48, 50-56 and 58-60 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

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DETAILED ACTION

Claims 31, 42, 50-53 and 55 have been amended. Claim 49, drawn to non-elected species, remains withdrawn from consideration. Claims 31-43, 45-48, 50-56, and 58-60 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claims 45-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "said administration" in claim 45 lacks antecedent basis in claim 41.

The rejection of claims 42, 43, 48, 50-56 and 58-60 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons of record.

Claims 50-54 are drawn in part to a genus comprising proteins having at least 70% homology to amino acid residues 384-641 of SEQ ID NO:1. Claims 42, 43, 45-48, 55, 56 and 58-60 are drawn in part to method claims for the in vivo activation of the "immune system" in a patients comprising the administration of proteins having at least 70% homology to amino acid residues 384-641 of SEQ ID NO:1. The specification sets forth Hsp70 as SEQ ID NO:1, and teaches that residues 384-641 of SEQ ID NO:1 are responsible for the activation of NK cells into cytotoxic cells. The specification teaches that the Hsp70 protein is a heat shock protein which is differentially expressed on many types of cancerous cells. The specification contemplates methods of activating NK cells by means of proteins having at least 70% homology to amino acid residues 384-681 of SEQ ID NO:1, wherein contacting of NK cells with an uncomplexed fragment of amino acid residues 384-641 of SEQ ID NO:1 stimulates the proliferation of NK cells and increases the cytolytic activity of NK cells. The method of claims 42, 43, 45-48, 55, 56

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and 58-60 are not limited to the direct increase in cytolytic activity of NK cells or the increase in proliferation of NK cells by contact with the variant fragment of Hsp70. thus, the genus of proteins encompassed by the method claims is highly variant because the administered fragment of Hsp70 having at least 70% homology to hsp70 need not have the same functional requirement of directly activating NK cells. The proteins encompassed by the claims could serve to activate dendritic cells or B cells or T cells, all of which would satisfy the specific limitation of activating the "immune response". The genus of proteins encompassed by claims 50-54 drawn to proteins having at least 70% homology with residues 384-681 of SEQ ID NO:1 is not limited by the functional attributes of the variant fragment. Thus, when given the broadest reasonable interpretation, the genus of variant Hsp70 fragments is variant encompassing widely ranging structural deviations from Hsp70 and the amino acid sequence comprising residues 384-681 of SEQ ID NO:1, wherein said deviations could include fusions with any other amino acid sequence, alterations of the protein backbone, coupling with any known chemical which reacts with amino acid sequences, proteolytic fragments of the amino acid sequence comprising residues 384-641 of SEQ ID NO:1, enzymatic modification of said amino acid sequence, and amino acid substitutions, deletions and additions to residues 381-641 of SEQ ID NO:1. The disclosure of SEQ ID NO:1 is inadequate written description for this multitude of species encompassed by the claims..

Applicant argues that the grounds of this rejection are both factually and legally flawed because applicant has provided the structure of the claimed variant by stating that said variant must have 70% homology to hsp70. this has been considered but not found persuasive. Applicant has not provided functional characteristics of the claimed variant. The M.P.E.P. requires the examiner to take the broadest reasonable interpretation and not "read in" limitations described in the specification. Applicant further argues that the examiners interpretation of the written description requirement is flawed because the courts have states that an adequate written description requires a description of the DNA itself. this has been considered but not found persuasive. Contemplating a fragment having 70% identity to hsp70 is not the same as providing a sequence of a variant fragment having 70% identity to hsp70. Applicant has therefore not provided "the DNA itself". Applicant cites the USPTO guidelines for written description, especially example 14 which states that variants having 95% identity to a reference sequence and

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also possess catalytic activity are anticipated by the description of SEQ ID NO:3. This has been considered but not found persuasive. The fact pattern in Example 14 is not the same fact pattern as in the instant rejected claims. Claims 50-54 are compositions which are not limited by a functional attribute (i.e. catalytic activity, or in the instant case, direct activation of NK cells). Claims 42, 43, 45-48, 55, 56 and 58-60 are broadly drawn to methods of activating an "immune response" which are not limited to the activation of NK cells.

Claims 50-53 are rejected under 35 U.S.C. 102(b) as being anticipated by Jindal et al (Bio/Technology, 1995, vol. 13, pp. 1105-1109). Jindal et al discloses isolated, purified recombinant human Hsp70 eluted by a NaCl solution from a Superdex 200 column equilibrated with HEPES (page 1108, second column, under the heading "Size Exclusion Chromatography"). Both HEPES and NaCl are pharmaceutically acceptable diluents.

The rejection of claims 55 and 56 under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 19 and 20 of U.S. Patent No. 6,261,839 is withdrawn in light of applicants amendments..

All other rejections and objections as set forth in the previous Office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828.

The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

Karen A. Canella
KARENA CANELLA PH.D.
PRIMARY EXAMINER